Air-stable, Storable, and Highly Selective Chiral Lewis Acid Catalyst

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Supporting Information

Experimental Section

General: Optical rotations were recorded on a JASCO P-1010 digital polarimeter. Melting points were measured on YAZAWA MICROMERTING POINT BY-1. IR spectra were recorded on a JASCO FT/IR-610 infrared spectrometer. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-LA300, JNM-LA400, or JNM-LA500 spectrometer in CDCl_3 . Tetramethylsilane (TMS) served as internal standard ($\delta = 0$) for ^1H NMR, and CDCl_3 was used internal standard ($\delta = 77.0$) for ^{13}C NMR. When dichloromethane- d_2 was used, dichloromethane- d_2 served as internal standard ($\delta = 5.32$) for ^1H NMR, and $\delta = 53.8$ for ^{13}C NMR. High performance liquid chromatography (HPLC) was carried out using following apparatuses; liquid chromatograph SHIMADZU LC-10AT (liquid chromatograph), and SHIMADZU SPD-10A (UV detector), and SHIMADZU C-R6A or C-R8A (chromatopac). Fluorescence X-ray analysis was measured with SHIMADZU Rayny EDX-800. Column chromatography was performed on Silica gel 60 (Merck) and preparative thin-layer chromatography was carried out using Wakogel B-5F. Dichloromethane was distilled from P_2O_5 , then from CaH_2 , and dried over MS 4A. All other solvents and chemical compounds were purified based on standard procedures.

Molecular sieves 3A, 4A, and 5A (powder) were purchased from Aldrich Co., Ltd. and dried ($200\text{ }^\circ\text{C}$, $<0.05\text{ mmHg}$, 8 h) before use. $\text{Zr}(\text{O}^t\text{Bu})_4$ was purchased from

Trichemical Laboratory Co., Ltd. *N*-Methylimidazole was purchased from Tokyo Kasei Kogyo Co., Ltd. Aldimines of aromatic aldehydes and heteroaromatic aldehydes were prepared from the corresponding aldehydes and 2-aminophenol by usual methods. The crude aldimines were recrystallized from ethanol to give the pure materials. Ketene silyl acetals were prepared according to the literature.¹ (*R*)-6,6'-C₂F₅BINOL² and (*R*)-3,3'-BrBINOL³ were prepared according to the literature. All reactions were carried out under argon atmosphere in dried glassware.

Preparation of ZrMS: To a suspension of powdered MS 5A (240 mg) in benzene (0.5 mL) were added (*R*)-6,6'-bis(pentafluoroethyl)-1,1'-bi-2-naphthol ((*R*)-6,6'-C₂F₅BINOL, 35.5 mg, 0.08 mmol) in benzene (0.5 mL), *N*-methylimidazole (NMI, 13.1 mg, 0.16 mmol) in benzene (0.5 mL), and Zr(O^{*i*}Bu)₄ (15.3 mg, 0.04 mmol) in benzene (0.5 mL) at room temperature. The mixture was stirred and heated at 80 °C for 2 h. After removal of the solvent under reduced pressure (0.05 mmHg) at 50 °C for 1 h, a *chiral zirconium catalyst with powdered molecular sieves* (ZrMS) was formed. ZrMS was handled in air and stored at ambient temperature.

A typical experimental procedure for the enantioselective Mannich reactions using ZrMS: A typical experimental procedure is described for the reaction of aldimine **1a** with ketene silyl acetal **2a**. To a suspension of ZrMS (0.02 mmol) in dichloromethane (0.3 mL) was added *N*-methylimidazole (0.04 mmol) in dichloromethane (0.2 mL) at room temperature. The mixture was stirred for 0.5 h at the same temperature and then cooled to -45 °C. Dichloromethane solutions (1.0 mL) of **1a** (0.2 mmol) and **2a** (0.24 mmol) were successively added. The mixture was stirred for 18 h, and saturated aq. NaHCO₃ was then added to quench the reaction. The aqueous layer was extracted with dichloromethane, and the crude adduct was treated with THF/1N HCl (10:1) at 0 °C for 30 min. After usual work-up, the crude product was chromatographed on silica gel to give the desired adduct **3a**. The optical purity was determined by HPLC analysis using a chiral column (see below).

(R)-Methyl 2,2'-dimethyl-(2-hydroxyphenyl)amino-3-phenylpropionate
(3a): $[\alpha]_{\text{D}}^{24} +1.4$ (*c* 1.15, CHCl₃)(87% ee). Mp 112.5-114 °C. IR (KBr): 3401, 1709, 1611, 1514, 1453, 1391 cm⁻¹. ¹H NMR: δ 1.21 (s, 3H), 1.24 (s, 3H), 3.68 (s, 3H), 4.57 (s, 1H), 6.36 - 6.76 (m, 4H), 7.21-7.28 (m, 5H). ¹³C NMR: δ 19.9, 24.2, 47.3, 52.3, 64.3, 113.2, 114.1, 117.6, 120.8, 127.3, 127.9, 128.3, 135.6, 138.9, 144.0, 178.0. HPLC: Daicel Chiralpak AD, hexane/*i*PrOH = 9/1, flow rate = 1.0 ml/min: *t*_R = 9.3 min (3*R*), *t*_R = 16.0 min (3*S*). Anal. Calcd for C₁₈H₂₁NO₃: C, 72.22; H, 7.07; N, 4.68. found: C, 72.28; H, 7.20; N, 4.62. HRMS: Calcd for C₁₈H₂₁NO₃ (M⁺) 299.1522, found 299.1497.

(R)-Methyl 2,2'-dimethyl-3-(2-hydroxyphenyl)amino-3-(1'-naphthyl)-propionate (Table 3, Entry 2): $[\alpha]_{\text{D}}^{24} +187.8$ (*c* 0.52, CHCl₃)(90% ee). Mp 135-136 °C. IR (neat): 3052, 1691, 1604, 1578, 1270, 798 cm⁻¹. ¹H NMR: δ 1.18 (s, 3H), 1.25 (s, 3H), 3.66 (s, 3H), 5.62 (s, 3H), 6.28-6.62 (m, 4H), 7.22-8.00 (m, 7H). ¹³C NMR: δ 19.9, 25.1, 48.4, 52.4, 57.8, 113.4, 114.2, 117.9, 121.2, 122.1, 123.2, 125.2, 125.3, 125.4, 126.1, 128.1, 129.1, 133.6, 135.3, 135.5, 144.1, 177.9. HPLC: Daicel Chiralcel OD, hexane/*i*PrOH = 19/1, flow rate = 0.8 ml/min: *t*_R = 25.8 min (3*S*), *t*_R = 29.0 min (3*R*). Anal. Calcd for C₂₂H₂₃NO₃: C, 75.62; H, 6.63; N, 4.01. found: C, 75.48; H, 6.49; N, 3.94. HRMS: Calcd for C₂₂H₂₃NO₃ (M⁺) 349.1678, found 349.1668.

(R)-S-Ethyl 3-(2-hydroxyphenyl)amino-3-phenylpropanethioate (Table 3, Entry 3): $[\alpha]_{\text{D}}^{24} +4.0$ (*c* 1.19, CHCl₃)(96% ee). Mp 79.5-80.5 °C. IR (KBr): 3396, 1647, 1608, 1520, 1449, 1362 cm⁻¹. ¹H NMR: δ 1.67 (t, 3H, *J* = 7.3 Hz), 2.83 (q, 2H, *J* = 7.3 Hz), 2.97 (dd, 1H, *J* = 5.4, 14.9 Hz), 3.07 (dd, 1H, *J* = 8.1, 14.9 Hz), 4.81 (dd, 1H, *J* = 5.4, 8.1 Hz), 6.44-6.71 (m, 4H), 7.20-7.33 (m, 5H). ¹³C NMR: δ 14.4, 23.6, 51.4, 56.1, 114.4, 114.6, 118.8, 121.1, 126.3, 127.4, 128.6, 134.9, 141.7, 144.7, 198.4. HPLC: Daicel Chiralpak AS, hexane/*i*PrOH = 19/1, flow rate = 1.0 ml/min: *t*_R = 26.6 min (3*S*) *t*_R = 38.2 min (3*R*). Anal. Calcd for C₁₇H₁₉NO₂S: C, 67.74; H, 6.35; N, 4.65. found: C, 68.00; H, 6.54; N, 4.54. HRMS: Calcd for C₁₇H₁₉NO₂S (M⁺) 301.1138, found 301.1102.

(R)-S-Ethyl 3-(2-hydroxyphenyl)amino-3-(1'-naphthyl)propane thioate (Table 3, Entry 4): $[\alpha]_D^{24} +127.7$ (*c* 2.47, CHCl₃)(90% ee). Mp 40.5-41.5 °C. IR (KBr): 3380, 1645, 1605, 1514, 1446, 1362, cm⁻¹. ¹H NMR: δ 1.18 (t, 3H, *J* = 7.3 Hz), 2.86 (q, 2H, *J* = 7.3 Hz), 3.03 (dd, 1H, *J* = 9.4, 14.8 Hz), 3.20 (dd, 1H, *J* = 3.3, 14.8 Hz), 5.68-5.70 (m, 1H), 6.30-6.71 (m, 4H), 7.29-8.23 (m, 7H). ¹³C NMR: δ 14.4, 23.7, 50.7, 51.9, 113.5, 114.4, 118.1, 121.3, 122.1, 123.1, 125.6, 125.7, 126.5, 128.0, 129.2, 130.3, 134.0, 135.3, 136.7, 143.9, 198.5. HPLC: Daicel Chiralpak AD, hexane/*i*PrOH = 9/1, flow rate = 1.0 ml/min: *t*_R = 15.5 min (3*S*), *t*_R = 21.0 min (3*R*). Anal. Calcd for C₂₁H₂₁NO₂S: C, 71.76; H, 6.02; N, 3.99. found: C, 71.94; H, 6.17; N, 3.81. HRMS: Calcd for C₂₁H₂₁NO₂S (M⁺) 351.1294, found 351.1287.

(R)-S-Ethyl 3-(4'-chlorophenyl)-3-[(2'-hydroxyphenyl)amino]propane thioate (Table 3, Entry 5): $[\alpha]_D^{24} +5.4$ (*c* 1.01, CHCl₃)(94% ee). IR (neat): 3412, 1665, 1610, 1516, 1447, 742 cm⁻¹. ¹H NMR: δ 1.21 (t, 2H, *J* = 7.4 Hz), 2.87 (q, 2H, *J* = 7.4 Hz), 2.96 (dd, 1H, *J* = 5.1, 14.9 Hz), 3.05 (dd, 1H, *J* = 8.3, 14.9 Hz), 4.78 (dd, 1H, *J* = 5.1, 8.3 Hz), 6.39-6.78 (m, 4H), 7.22-7.28 (m, 4H). ¹³C NMR: δ 14.5, 23.7, 51.2, 55.6, 114.5, 115.0, 119.3, 121.2, 127.8, 128.9, 133.2, 134.6, 140.3, 144.7, 197.8. HPLC: Daicel Chiralpak AD, hexane/*i*PrOH = 9/1, flow rate = 1.0 ml/min: *t*_R = 19.5 min (3*S*), *t*_R = 24.3 min (3*R*). Anal. Calcd for C₁₇H₁₈NO₂ClS: C, 60.80; H, 5.40; N, 4.17. found: C, 60.85; H, 5.60; N, 3.99. HRMS: Calcd for C₁₇H₁₈NO₂ClS (M⁺) 335.0750, found 335.9758.

(S)-S-Ethyl 3-(2'-furyl)-3-[(2'-hydroxyphenyl)amino]propanethioate (Table 3, Entry 6): $[\alpha]_D^{23} -17.6$ (*c* 1.01, CHCl₃)(89% ee). IR (neat): 3414, 1674, 1608, 1513, 1448, 1349, 740 cm⁻¹. ¹H NMR: δ 1.32 (t, 3H, *J* = 7.3 Hz), 2.90 (q, 2H, *J* = 7.3 Hz), 3.06 (dd, 1H, *J* = 5.4, 15.6 Hz), 3.19 (dd, 1H, *J* = 8.3, 15.6 Hz), 4.81 (dd, 1H, *J* = 5.4, 8.3 Hz), 6.11 (d, 1H, *J* = 3.2 Hz), 6.26 (dd, 1H, *J* = 2.0, 3.2 Hz), 6.60-6.81 (m, 4H), 7.35 (d, 1H, *J* = 2.0 Hz). ¹³C NMR: δ 14.5, 23.6, 48.0, 50.8, 106.8, 110.2, 115.0, 118.0, 120.7, 121.5, 133.8, 142.0, 147.1, 153.8, 198.2. HPLC: Daicel Chiralcel OD, hexane/*i*PrOH = 9/1, flow rate = 1.0 ml/min: *t*_R = 13.4 min (3*S*), *t*_R = 24.5 min (3*R*). Anal. Calcd for C₁₅H₁₇NO₃S: C, 61.83; H, 5.88; N, 4.81. found: C,

61.86; H, 5.72; N, 4.80. HRMS: Calcd for C₁₅H₁₇NO₃S (M⁺) 291.0932, found 291.0931.

When using the aliphatic imine from isovaleraldehyde instead of an aromatic imine, the imine preparation and the Mannich reaction were performed as follows. To a suspension of ZrMS (0.02 mmol) in dichloromethane (0.3 mL) were added *N*-methylimidazole (0.04 mmol) in dichloromethane (0.2 mL) at room temperature. The mixture was stirred for 0.5 h, and then 2-amino-*m*-cresol (0.2 mmol) and isovaleraldehyde (0.3 mmol) in dichloromethane (0.5 mL) were added at the same temperature. The mixture was further stirred for 0.5 h, cooled to -45 °C, and a dichloromethane solution (0.5 mL) of **2b** (0.3 mmol) was added. The mixture was stirred for 18 h, and saturated aq. NaHCO₃ was then added to quench the reaction. The aqueous layer was extracted with dichloromethane, and the crude adduct was treated with THF/1N HCl (10:1) at 0 °C for 30 min. After usual work-up, the crude product was chromatographed on silica gel to give the desired adduct.

(R)-S-Ethyl 3-[(2-hydroxy-6-methylphenyl)amino]-5-methylhexane-thioate (Table 3, Entry 7): [α]_D²⁶ +14.1 (*c* 0.91, CHCl₃)(92% ee). IR (neat): 3356, 2957, 2871, 1681, 1588, 1472, 1366 cm⁻¹. ¹H NMR: δ 0.81 (d, 3H, *J* = 6.4 Hz), 0.88 (d, 3H, *J* = 6.6 Hz), 1.26 (t, 3H, *J* = 7.4 Hz), 1.35 (dd, 2H, *J* = 6.6, 7.7 Hz), 1.63 (7, 1H, *J* = 6.7 Hz), 2.25 (s, 3H), 2.64 (dd, 1H, *J* = 8.0, 15.9 Hz), 2.80 (dd, 1H, *J* = 4.2, 15.8 Hz), 2.92 (q, 2H, *J* = 7.5 Hz), 3.62 (dq, 1H, *J* = 4.2, 7.1 Hz), 6.66 (dd, 1H, *J* = 0.6, 7.4 Hz), 6.76 (dd, 1H, *J* = 1.4, 7.8 Hz), 6.88 (t, 1H, *J* = 7.7 Hz). ¹³C NMR: δ 14.6, 18.1, 22.0, 23.2, 23.6, 25.1, 44.5, 48.4, 52.5, 113.3, 121.8, 124.6, 131.2, 132.5, 151.9, 200.3. HPLC: Daicel Chiralpak OD, hexane/*i*PrOH = 60/1, flow rate = 1.0 ml/min: *t*_R = 14.9min (3*S*), *t*_R = 17.2 min (3*R*). Anal. Calcd for C₁₆H₂₅NO₂S: C, 65.05; H, 8.53; N, 4.74. found: C, 65.28; H, 8.26; N, 4.93.

The optical purity of isopropyl 2-*tert*-butyldimethylsiloxy-3-(2-hydroxyphenyl) amino-3-phenylpropionate was determined after methylation of the phenolic OH group.

Isopropyl 2-*tert*-butyldimethylsiloxy-3-(2-methoxyphenyl)amino-3-phenylpropionate (Table 3, Entry 8; methylated, *syn/anti* mixture) IR (neat): 3426, 2935, 1752, 1603, 1519, 1457, 1106 cm⁻¹. ¹H NMR *syn*: δ 0.00 (s, 6H), 0.93 (s, 9H), 1.23 (d, 3H, *J* = 6.3 Hz), 1.30 (d, 3H, *J* = 6.3 Hz), 3.97 (s, 3H), 4.48 (d, 1H, *J* = 3.0 Hz), 4.97 (dd, 1H, *J* = 3.0, 7.6 Hz), 5.11 (dq, 1H, *J* = 6.3 Hz), 5.53 (d, 1H, *J* = 7.6 Hz), 6.38 (dd, 1H, *J* = 1.7, 7.6 Hz), 6.54 - 6.85 (m, 3H), 7.26 - 7.46 (m, 5H). *anti*: δ = 0.03 (s, 3H), 0.06 (s, 3H), 1.00 (s, 9H), 1.13 (d, 3H, *J* = 6.3 Hz), 1.26 (d, 3H, *J* = 6.3 Hz), 3.93 (s, 3H), 4.61 (d, 1H, *J* = 5.3 Hz), 4.83 (dd, 1H, *J* = 5.3, 8.3 Hz), 5.00 (dq, 1H, *J* = 6.3 Hz), 5.38 (d, 1H, *J* = 8.3 Hz), 6.54 - 6.85 (m, 4H), 7.26 - 7.46 (m, 5H). ¹³C NMR *syn*: δ -5.9, -5.3, 18.1, 21.6, 21.7, 25.5, 55.5, 60.2, 68.6, 76.8, 109.5, 111.1, 116.2, 121.1, 127.2, 127.9, 128.2, 136.8, 140.0, 146.9, 171.2. *anti*: δ = -5.9, -5.2, 18.2, 21.5, 21.6, 25.6, 55.2, 59.8, 55.2, 59.8, 68.5, 75.4, 109.3, 111.1, 116.6, 121.1, 127.5, 127.7, 128.5, 136.3, 138.1, 147.0, 171.1. HRMS: C₂₅H₃₇NO₄Si 443.2493, obsd. 443.2485. HPLC: Daicel CHIRALPAK ADx2; Hexane / *i*PrOH = 400 / 1; flow 0.8 ml/min: *t*_R = 21.7 (2*S*,3*R*), 25.7 (2*R*,3*S*).

Phenyl 2-benzyloxy-3-(2-hydroxyphenyl)amino-3-phenylpropionate (Table 3, Entry 9; *syn/anti* = 8/92): IR (neat): 3420, 1754, 1610, 1593, 1514, 1493, 1454, 1266 cm⁻¹. ¹H NMR *anti*: δ 4.51 (d, 1H, *J* = 11.7 Hz), 4.56 (d, 1H, *J* = 5.4 Hz), 4.78 (d, 1H, *J* = 11.7 Hz), 4.95 (d, 1H, *J* = 5.4 Hz), 6.51-6.73 (m, 4H), 6.80-6.92 (m, 2H), 7.12-7.20 (m, 2H), 7.24-7.28 (m, 6H), 7.33 (s, 3H), 7.43-7.45 (m, 2H). *syn*: δ 4.45 (d, 1H, *J* = 12.1 Hz), 4.74 (d, 1H, *J* = 3.9 Hz), 4.80 (d, 1H, *J* = 12.1 Hz), 5.08 (brd, 1H, *J* = 3.9 Hz), 6.51-6.73 (m, 4H), 6.80-6.92 (m, 2H), 7.12-7.20 (m, 2H), 7.24-7.28 (m, 6H), 7.33 (s, 3H), 7.43-7.45 (m, 2H). ¹³C NMR *anti*: δ 59.8, 73.2, 80.6, 114.1, 114.5, 118.7, 119.0, 121.1, 121.2, 121.2, 126.0, 127.9, 128.1, 128.3, 128.4, 128.4, 129.3, 136.7, 138.3, 144.4, 150.0, 169.6. *syn*: δ 60.7, 73.0, 79.6, 113.4, 115.3, 117.7, 118.4, 120.4, 121.1, 121.3, 125.9, 128.0, 128.1, 128.2, 128.3, 128.5, 129.2, 136.4, 136.5, 144.3, 149.8, 169.5. HPLC: Daicel Chiralcel OD, hexane/*i*PrOH = 19/1, flow rate = 1.0 ml/min: *t*_R = 20.0 min (2*R*,3*S*), *t*_R = 24.5 min (2*S*,3*R*), *t*_R = 29.5 min (2*S*,3*S*), *t*_R = 32.1 min (2*R*,3*R*). HRMS: Calcd for C₂₈H₂₅NO₄ (M⁺) 439.1784, found 439.1774.

NMR experiments (Figure 1): The samples for the NMR experiments were prepared according to the following methods.

Sample (a): After a suspension of ZrMS (0.04 mmol) in dichloromethane- d_2 (1.0 mL) was stirred for 0.5 h at room temperature, MS 5A was filtered off to prepare the NMR sample.

Sample (b): To a benzene- d_6 solution (0.5 ml) of (*R*)-6,6'- C_2F_5 BINOL (0.08 mmol) was added a benzene- d_6 solution (0.5 ml) of $Zr(O^tBu)_4$ (0.04 mmol) at room temperature. The mixture was stirred and heated at 80 °C for 2 h, and then evaporated and dried under reduced pressure (0.05 mmHg) at 50 °C for 1 h. The sample for the NMR experiment was prepared using dichloromethane- d_2 as a solvent.

Sample (c): To a suspension of ZrMS (0.04 mmol) in dichloromethane- d_2 (0.6 mL) were added *N*-methylimidazole (0.08 mmol) in dichloromethane- d_2 (0.4 mL) at room temperature. After the mixture was stirred for 0.5 h at the same temperature, MS 5A was filtered off to prepare the NMR sample.

Sample (d): To a benzene- d_6 (0.5 ml) solution of (*R*)-6,6'- C_2F_5 BINOL (0.08 mmol) and *N*-methylimidazole (0.16 mmol) was added a benzene- d_6 solution (0.5 ml) of $Zr(O^tBu)_4$ (0.04 mmol) at room temperature. The mixture was stirred and heated at 80 °C for 2 h, and then evaporated and dried under reduced pressure (0.05 mmHg) at 50 °C for 1 h. The sample for the NMR experiment was prepared using dichloromethane- d_2 as a solvent.

Preparation of another ZrMS prepared using (*R*)-3,3'-BrBINOL as a ligand: To a solution of (*R*)-3,3'-dibromo-1,1'-bi-2-naphthol ((*R*)-3,3'-BrBINOL, 17.8 mg, 0.04 mmol) in THF (1.0 mL) was added $Zr(O^tBu)_4$ (15.3 mg, 0.04 mmol) in THF (0.5 mL) at room temperature. The mixture was stirred for 0.5 h, and water (1.4 mg, 0.08 mmol) in THF (0.5 mL) was then added. After the mixture was stirred for 0.5 h, powdered MS 3A (240 mg) was added. The suspension was stirred for 5 min, and the solvent was removed under reduced pressure (0.05 mmHg) at room

temperature for 1 h. Another ZrMS using (*R*)-3,3'-BrBINOL as a ligand was formed, and was treated in air and stored at ambient temperature.

A typical experimental procedure for the enantioselective Mannich reactions using another ZrMS using (*R*)-3,3'-BrBINOL as a ligand: A typical experimental procedure is described for the reaction of aldimine **1a** with ketene silyl acetal **2a**. To a suspension of ZrMS (0.02 mmol) in THF (0.5 mL) at -45 °C were added THF solutions (1.0 mL) of **1a** (0.2 mmol) and **2a** (0.24 mmol) successively. The mixture was stirred for 18 h, and saturated aq. NaHCO₃ was then added to quench the reaction. The aqueous layer was extracted with dichloromethane, and the crude adduct was treated with THF/1N HCl (10:1) at 0 °C for 30 min. After usual work-up, the crude product was chromatographed on silica gel to give the desired adduct **3a**. The optical purity was determined by HPLC analysis using a chiral column.

Recovery and reuse of ZrMS: To a suspension of ZrMS (0.04 mmol) in dichloromethane (0.6 mL) was added *N*-methylimidazole (0.08 mmol) in dichloromethane (0.4 mL) at room temperature. The mixture was stirred for 0.5 h at the same temperature and then cooled to -45 °C. Dichloromethane solutions (2.0 mL) of **1a** (0.4 mmol) and **2a** (0.48 mmol) were successively added. After 18 h, the reaction vessel was warmed to room temperature and MS 5A (240 mg) was added. After all volatile solvents and materials were removed under reduced pressure (3 h), hexane (5.0 mL) was added, and the mixture was stirred for 5 min. The hexane was removed by decantation, and the ZrMS was washed with hexane twice in the same way. 2-Naphthol (internal standard) was added to the combined hexane solutions, and leaching of the ligand was measured by HPLC analysis (5%). The hexane was evaporated, and leaching of the zirconium was measured by Fluorescence X-ray analysis (5%). Desired product **3a** was isolated from the residue after usual work-up (89% y, 92% ee). The recovered ZrMS was dried at room temperature under reduced pressure for 3 h and was used for the 2nd run.

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